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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,252	02/02/2001	Andrew Ellington	D6296	9740

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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,252	ELLINGTON, ANDREW	
	Examin r	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-12,15,19-25 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-12,15,19-25 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6/01* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 August 2003 has been entered.

Status of the Claims

2. The examiner for this application has changed. Please address further correspondence to BJ Forman, Art Unit: 1634.

3. This action is in response to papers filed 29 August 2003 in which claims 1, 6, 7, 10, 15, 20 and 28 were amended.

All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 26 November 2002 are withdrawn in view of the amendments and new grounds for rejection. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments and new grounds for rejection. New grounds for rejection are discussed.

Claims 2-5, 13-14, 16-18 and 26-27 are canceled.

Claims, 6-12, 15, 19-25 and 28 are under prosecution.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 6-12, 15, 19, 23, 25 and 28 are rejected under 35 U.S.C. 102(a) as being anticipated by Jayasena et al (WO 99/31276, published 24 June 1999).

Regarding Claim 1, Jayasena et al disclose a method of transducing a conformation change of a signaling aptamer that occurs upon the signaling aptamer binding a ligand to a detectable increased signal generated by a reporter molecules that is appended to the aptamer prior to binding, the method comprising, covalently coupling the reporter molecule (fluorescein phosphoramidite, page 43, lines 12-27) to forma the signaling aptamer wherein the reporter replaces a nucleic acid in the aptamer, placing the signaling aptamer in solution, contacting the signaling aptamer in solution with the ligand under conditions whereby the aptamer binds the ligand and detecting the increase in fluorescence intensity generated by the reporter molecule transduced by conformational change in the signaling aptamer upon binding the ligand (page 32, line 14-page 34, line 30).

Regarding Claim 6, Jayasena et al disclose the method wherein the covalent coupling of the reporter molecule occurs during chemical synthesis (page 43, lines 12-27).

Regarding Claims 7-9, Jayasena et al disclose the method wherein the reported is a fluorescent dye i.e. fluorescein (page 43, lines 12-13).

Regarding Claim 10, Jayasena et al disclose the method wherein the aptamer is selected from RNA, DNA, modified RNA and modified DNA i.e. nucleic acid ligand (page 16, line 6-page 17, line 15).

Regarding Claim 11, Jayasena et al disclose the method wherein the ligand is not a nucleic acid sequence i.e. target (page 16, lines 21-26 and page 17, lines 16-22).

Regarding Claim 12, Jayasena et al disclose the method wherein the ligand is in solution (page 15, lines 8-11).

Regarding Claim 15, Jayasena et al disclose a method of transducing a conformation change of a signaling aptamer that occurs upon the signaling aptamer binding a ligand to a detectable increased signal generated by a fluorescent dye that is appended to the aptamer prior to binding, the method comprising, covalently coupling the fluorescent dye (fluorescein phosphoramidite, page 43, lines 12-27) to forma the signaling aptamer wherein the dye replaces a nucleic acid in the aptamer, placing the signaling aptamer in solution, contacting the signaling aptamer in solution with the ligand under conditions whereby the aptamer binds the ligand and detecting the increase in fluorescence intensity generated by the reporter molecule transduced by conformational change in the signaling aptamer upon binding the ligand (page 32, line 14-page 34, line 30).

Regarding Claims 19, Jayasena et al disclose the method wherein the fluorescent dye is fluorescein (page 43, lines 12-13).

Regarding Claim 23, Jayasena et al disclose the method wherein the ligand is not a nucleic acid sequence i.e. target (page 16, lines 21-26 and page 17, lines 16-22).

Regarding Claim 25, Jayasena et al disclose the method wherein the ligand is in solution (page 15, lines 8-11).

Regarding Claim 28, Jayasena et al disclose the method wherein the ligand is quantitated by correlating the increased fluorescence generated upon ligand binding to the unbound ligand signal (page 30, lines 16-29).

6. Claims 1, 6-12, 15, 19, 23, 25 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Jayasena et al (U.S. Patent No. 6,531,286, filed 18 September 1998).

Regarding Claim 1, Jayasena et al disclose a method of transducing a conformation change of a signaling aptamer that occurs upon the signaling aptamer binding a ligand to a detectable increased signal generated by a reporter molecules that is appended to the aptamer prior to binding, the method comprising, covalently coupling the reporter molecule (fluorescein phosphoramidite, Column 29, lines 40-65) to form a the signaling aptamer wherein the reporter replaces a nucleic acid in the aptamer, placing the signaling aptamer in solution, contacting the signaling aptamer in solution with the ligand under conditions whereby the aptamer binds the ligand and detecting the increase in fluorescence intensity generated by the reporter molecule transduced by conformational change in the signaling aptamer upon binding the ligand (Column 23, lines 7-64 and Claim 1).

Regarding Claim 6, Jayasena et al disclose the method wherein the covalent coupling of the reporter molecule occurs during chemical synthesis (Column 29, lines 40-65).

Regarding Claims 7-9, Jayasena et al disclose the method wherein the reported is a fluorescent dye i.e. fluorescein (Column 29, lines 40-65).

Regarding Claim 10, Jayasena et al disclose the method wherein the aptamer is selected from RNA, DNA, modified RNA and modified DNA i.e. nucleic acid ligand (Column 11, lines 10-51).

Regarding Claim 11, Jayasena et al disclose the method wherein the ligand is not a nucleic acid sequence i.e. target (Column 11, lines 33-41 and Column 12, lines 5-15).

Regarding Claim 12, Jayasena et al disclose the method wherein the ligand is in solution (Column 10, lines 35-41).

Regarding Claim 15, Jayasena et al disclose a method of transducing a conformation change of a signaling aptamer that occurs upon the signaling aptamer binding a ligand to a detectable increased signal generated by a fluorescent dye that is appended to the aptamer prior to binding, the method comprising, covalently coupling the fluorescent dye (fluorescein phosphoramidite, Column 29, lines 40-65) to form a the signaling aptamer wherein the dye replaces a nucleic acid in the aptamer, placing the signaling aptamer in solution, contacting the signaling aptamer in solution with the ligand under conditions whereby the aptamer binds the ligand and detecting the increase in fluorescence intensity generated by the reporter molecule transduced by conformational change in the signaling aptamer upon binding the ligand (Column 23, lines 7-64 and Claim 1).

Regarding Claims 19, Jayasena et al disclose the method wherein the fluorescent dye is fluorescein (Column 29, lines 40-65).

Regarding Claim 23, Jayasena et al disclose the method wherein the ligand is not a nucleic acid sequence i.e. target (Column 11, lines 33-41 and Column 12, lines 5-15).

Regarding Claim 25, Jayasena et al disclose the method wherein the ligand is in solution (Column 10, lines 35-41).

Regarding Claim 28, Jayasena et al disclose the method wherein the ligand is quantitated by correlating the increased fluorescence generated upon ligand binding to the unbound ligand signal (Column 20, lines 57-67).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 20-22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jayasena et al (U.S. Patent No. 6,531,286, filed 18 September 1998) in view of Szostak et al. (U.S. Patent No. 5,631,146, issued 20 May 1997)..

Regarding Claims 20-22 and 24, the claimed method embodiment differs from the method of Jayasena et al wherein the aptamer is an anti-adenosine RNA or DNA aptamer wherein the former is ATP-R-ACI3 and the latter is DFL7-8 and the ligand (target molecules) is adenosine. However, Jayasena et al note that numerous diagnostically important nucleic acid ligands that bind target molecules have been identified (Column 2, line 53-Column 4, line 64). Furthermore, the Szostak et al. patent teaches anti-adenosine triphosphate and anti-adenosine DNA aptamers prepared by the same process (Column 4, line 56-column 6, line 9). It would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to employ an anti-adenosine aptamer in the method of Szostak et al in view of the Jayasena et al. teaching such aptamers (nucleic acid ligands) were known in the art and in view of the known benefit of employing an aptamer that was known and proven in the art and readily obtainable by synthesis of the published nucleotide sequence. It would have been obvious further to synthesize aptamer

analogues of the claims 21 and 22 aptamers in view of the teaching of Szostak et al. of a large number of anti-adenosine aptamers having the same conserved region as the aptamer of claim 22 (Figure 4A) and the methods for producing them wherein such aptamers would have been expected by one of ordinary skill in the art to function in the same manner as the aptamers of claims 21 and 22 in view of the reference teaching that the conserved regions are the critical adenosine binding regions (column 7, lines 29-35 and column 8, lines 47-52).

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
October 24, 2003